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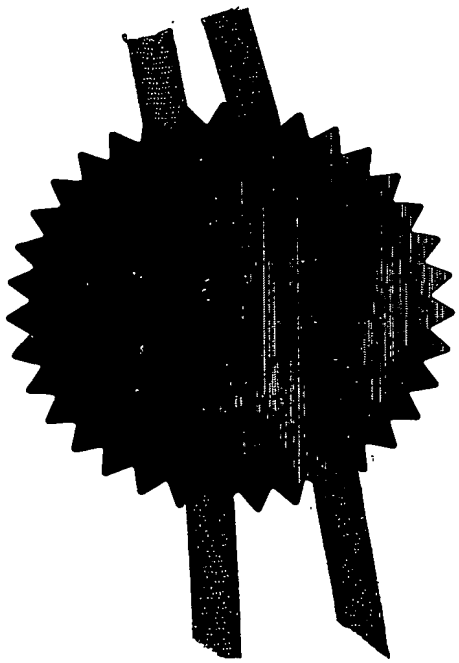

Signed

Dated 14 January 2004

Patents Form 1/77

The Patent Office

Patents Act 1977
(Rule 16)

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office
Cardiff Road
Newport
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1. Your reference IT/GM/N13395

2. Patent application number *(The Patent Office will fill this part)* 16 DEC 2002 0229274.6

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

ANSON MEDICAL LIMITED
67 Milton Park
Abingdon
OX14 4RX

07917552001

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation United Kingdom

4. Title of the invention

INSTRUMENT FOR TESTING PULSATILE ENDURANCE OF VASCULaR IMPLANTS

5. Name of your agent *(if you have one)*
"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

Williams Powell
4 St. Paul's Churchyard
London
EC4M 8AY

Patents ADP number *(if you know it)* 5830310001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority appliation number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earleir UK application, give the number and the filing date of the earlier application.

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(answer 'Yes if:*
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

YES

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	6
Claim(s)	9
Abstract	
Drawing(s)	1 + 1

10. If you are filing one of the following, state how many against each item.

Priority documents	
translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/we quest the grant of a patent on the basis of this application.

Signature LP Date 16/12/02

12. Name and daytime telephone number of person to contact in the United Kingdom — Mr Lee Anderson 020 7329 4400

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you form applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) ***If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505.***

b) *Write your answers in capital letters using black ink or you may type them.*

c) *If there is not enough space for all the relevant details on any part of this form, please continue on a sepate sheet of paper and write "see continuation sheet" in the relevant part(s). Any continuation sheet should be attached to this form.*

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Instrument for testing pulsatile endurance of vascular implants

Prosthetic vascular implants, such as heart-valves, stents, grafts and stent-grafts used for human implantation are subjected to the continuous fluctuating stress of blood pressure. It is therefore necessary to test such implants to prove their durability over a life time of exposure to pulsatile blood pressure.

Commercial machines are available from suppliers such as Enduratec Inc and Dynatek Dalta which provide one or more resilient tubes into which are placed samples of the implant. The tubes are filled with liquid, typically isotonic saline, and the pressure within the tube is varied by means of a pump. Different types of pump are used, some workers employ positive displacement mechanical pumps while others prefer electrically driven linear motors which drive pistons directly.

The fatigue process relies upon a first raised liquid pressure inside the tube expanding the tube and a second, lowered, liquid pressure allowing the tube to contract. As the tube expands, the radial resilience of the implant urges it to expand with the tube. As the tube contracts, it squeezes the implant back to its original size.

There are a number of common failures or difficulties associated with locating the implant within a test tube.

The most serious commercially is the consequence of a test-tube rupturing during the test. In most circumstances, the implant being tested is placed into the test tube by means of a catheter or similar tube. The implant is first crushed before passing through the catheter and this crushing process can severely affect the life expectancy of the implant. Thus, if the test-tube fails during a test, the test-tube itself can be replaced but it is not feasible to re-deliver the implant through a catheter. This is because it would involve crushing the implant into a catheter a second time and its life expectancy will consequently be reduced. The cost of replacing the implant is rarely important; however, endurance tests typically last between 3 months and 6 months and such a failure can easily delay testing, and therefore the time to launch a product, by several months.

As a consequence of the above failure mode, designers of test machines will usually employ a particularly tough test-tube with thick walls. The compliance of such a tube (ie the percentage increase in diameter per unit pressure) is relatively low, and in order to achieve changes in diameter which are physiologically representative, the pulsatile pressures used to inflate the tubes are usually significantly higher than physiological pressures. For instance, in the abdominal aorta, blood pressure in the average healthy subject is 120mm Hg / 80mm Hg, ie the blood pressure varies by 40mm Hg for every pulse. Compliance of a healthy aorta can be of the order of 5% per 100mm Hg so that a change in diameter of 2% can be expected at every heart beat. In order to simulate such a change in diameter, some workers employ a pulse pressure between 80mm Hg and 100mm Hg.

If the implant presents a significant surface area across the lumen of the vessel, such as a tapered stent or stent graft, then the force per unit area along the axis of the implant is increased in proportion with the inflation pressure of the test-tube. This elevated pressure induces failure modes such as limb separation or migration which would not occur at physiological pressures.

A shortcoming of existing designs unrelated to the failure described above lies in the limitation of the form of the test tube. Stent grafts frequently are designed for use in bifurcated vessels and require bifurcated test tubes for their testing. Stent-grafts are also intended for use in aneurysms, so that where the vessel is normal, parts of the implant will be in contact with the wall of the vessel whereas where the vessel is aneurysmal, the stent graft will be passing through a void. Moreover, diseased vessels are frequently highly tortuous. As a result of these factors, test tubes must be available that bifurcate, that have different compliance in different places, that can be aneurysmal and which are highly tortuous. The production of such complex test tubes is, where it is even possible, difficult, expensive and time consuming.

A further issue in endurance testing arises from the need to complete life-time tests in a commercially appropriate period of time. Typically, vascular implants are tested for

400,000,000 cycles which represent approximately 10 years of implantation life at a heart rate of 80 beats per minute. Many companies test large implants at approximately 35 Hz, allowing testing to be completed in approximately 19 weeks.

It is desirable to increase the speed of testing by as much as possible in order to accelerate the time taken to market a new product. However, the testing method described above has a frequency limit which arises from the radial resilience and the surface area of the implant. This arises from the following mechanism:

When the pressure in the test-tube is increased, it moves away from the walls of the implant. The radial resilience of the implant urges the wall of the implant to follow the wall of the test tube, however, the resilient force may not be sufficient to overcome the drag of the wall through the fluid for it to move as quickly as the wall of the test tube. Thus, where the drag is high, the radial resilience low and the testing speed is also high, the vascular implant can lag behind the movement of the wall of the test tube. In these circumstances, the strain induced in the implant reduces as the frequency increases and the change in diameter of the implant no longer matches the change in diameter of the test-tube.

The present invention relates to an improved arrangement for testing vascular implants which overcomes or minimises all of the limitations described above. The improved technique employs a test tube which is deployed inside the vascular implant, the test tube being made of a resilient material such as latex rubber, silicone rubber, poly-urethane or similar. Preferably, the test tube is made with very thin walls so that inflation pressures within the tube are transferred directly to the inner surface of the implant under test. In practice, contraceptive condoms provide an ideal tube for testing larger implants.

Such an arrangement has the advantage that should the test tube break during the test, a replacement tube can be threaded through the implant without risk of damage to the implant. In this way, failure of a test tube will never automatically require the test implant to be rejected nor lose the testing time taken up to the moment of failure.

A second benefit of such an arrangement is that physiological pressures can be used within the test tube because there is very little attenuation of the pressure by the very thin walls.

A third benefit of such a system is that the mechanical properties of the vessel surrounding the implant under test can be varied at different points and the vessel can even be made of separate components because there is no longer a requirement that the outer tube be fluid-tight. This allows the compliance of different regions to be optimised without the requirement that the entire 'vessel' is made from the same material.

A fourth benefit of the such a system is that the internal test tube is very soft and this permits the test implant to be bent or angled severely, purely by means of restraints, rather than requiring a custom made, angled test tube.

A fifth benefit of the system allows the test frequency to be increased because the implant is driven internally to expand rather than relying upon its radial resilience. When used in combination with an outer tube, the above described system provides a positively driven method of expanding an implant and additional resilience from the outer tube to compress an implant. The movement of the wall of the implant is then much less dependent upon the characteristics of the implant alone and testing can be carried out at frequencies of 50 Hz to 100 Hz. At this speed, testing to 400 million cycles can be completed in 7 weeks.

The diameters of implant that can be accommodated by such a machine lie in the range 2mm to 50mm, although if having sufficiently thin walls, the inner test tube can be significantly under- or over-sized.

The wall thickness of the inner tube preferably lies in the range 0.03 mm to 0.2 mm, although with loss in performance, some benefits of the inner tube can still be gained if the wall thickness is several millimetres.

Figure 1 illustrates the arrangement of a practical machine set up to test bifurcated implants which comprises:

A supporting gantry (1).
Inlet tubes (2).
Vascular implant (3).
Inner test-tubes (4).
Short outer test tube to reduce compliance at the neck of the implant (5).
Bungs (6) and (7).

This arrangement exploits ultra-thin walled condoms used as a pair to fill the single main body of the implant and the twin legs. In order to allow higher pressures to be used within the condom, bungs (6) and (7) are used to limit the extent to which the inner test-tube can expand length-wise. At each exit to the vascular implant, this limit is arranged to lie within a portion of outer tube which runs continuously to the vascular implant. In this way, there is no path for the inner test-tube to expand or herniate beyond the vascular sample or outside the outer test tube. This limits the ultimate strain put on the inner tube and prevents it from bursting unless very high pressures are employed.

A further improvement employed in this arrangement is the use of compressed air as the pressurising medium for the inner tubes. In order to make the air pressure pulsatile, a rotating valve or oscillating piston can be used and the design of such a valve or piston is greatly simplified by only being required to modulate the pressure of air. Other workers using saline filled systems generally require the pressure modulator to operate directly on salt water which involves the problems of corrosion and leakage.

A further benefit of employing air to pressurise the system is that the mass of oscillating fluid is significantly reduced over using saline. This in turn reduces the power required of the modulating system.

In order to employ an air pressurised system, it is still necessary that the vascular implant is maintained at physiological temperatures and in saline. Where the outer tube is discontinuous, the implant can be kept in saline by placing the entire system in a bath of salt water at an appropriate temperature.

In large implants, the change in volume per pressure pulse can be large and places significant demands on the modulator. Compressed air systems are more demanding than liquid-filled systems in this respect because of the compressibility of the gas. In order to reduce the volume of gas in such a system, the test-tubes can be part-filled with water and small bore tubes can be used.

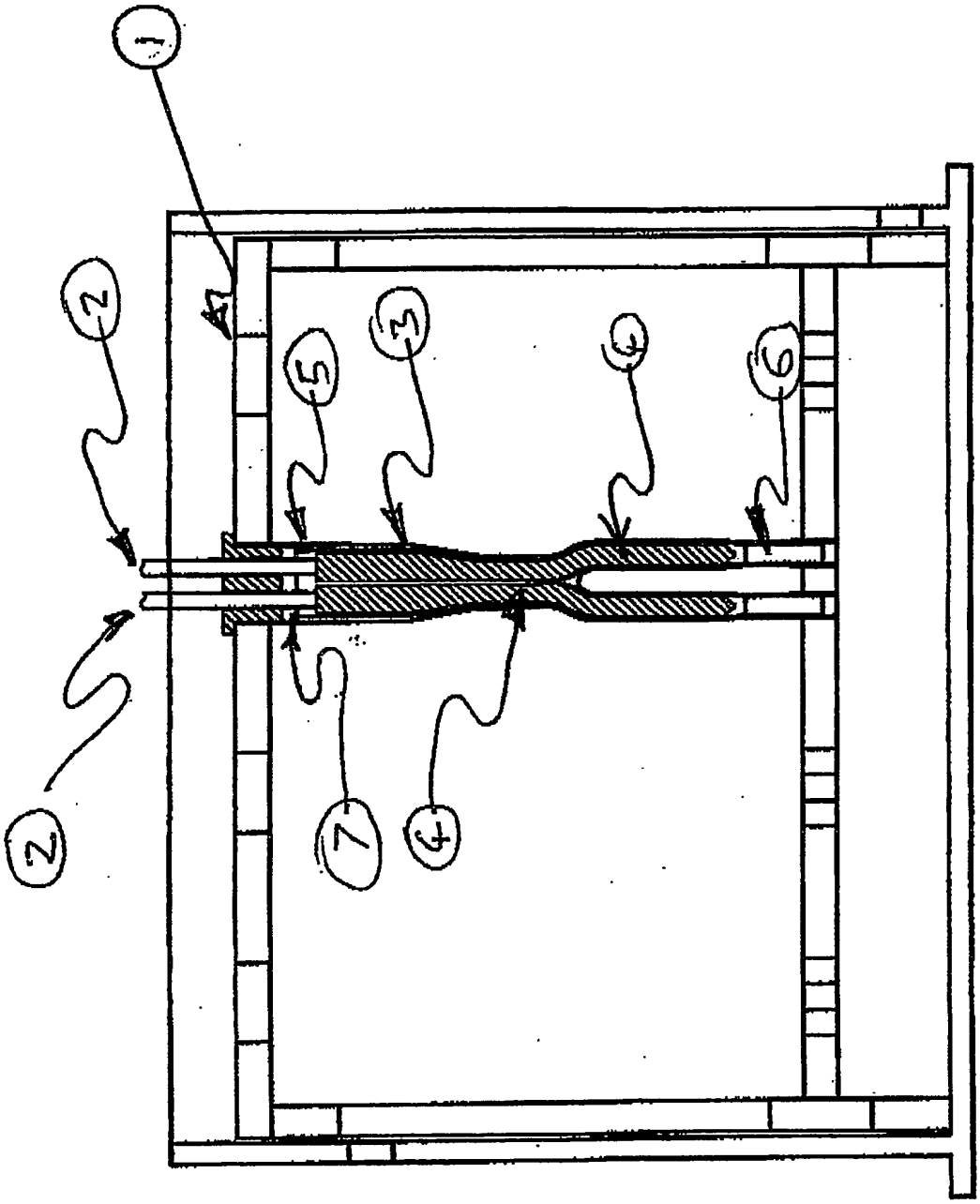

FIG. 1